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Case Report

Hyper IgE syndrome (hies; job syndrome): A case report

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Abstract

The hyper-immunoglobulin E syndrome (HIES) is a rare primary immunodeficiency disorder characterized by high serum levels of immunoglobulin E (IgE), recurrent cutaneous and pulmonary infections, chronic dermatitis and a variety of connective tissue and skeletal abnormalities. These patients share characteristic facial appearance and many oral manifestations. We report a case of hyper IgE syndrome (HIES) also known as "Job syndrome".

Keywords: Hyper-immunoglobulin E syndrome, Job syndrome, Primary immunodeficiency, Eosinophilia, Recurrent infections.

Introduction

The hyper-immunoglobulin E syndrome (HIES) is a rare primary immunodeficiency disorder characterized by recurrent cutaneous and pulmonary infections, eczematous dermatitis and elevated serum IgE concentrations[1-3]. In 1966, Davis et al described this disease first as "Job's syndrome" in two girls suffering from recurrent "cold" staphylococcal abscesses, pneumonia and neonatal-onset eczematous rash[4]. In 1972, Buckley et al.[5] found extremely high serum IgE levels in these patients. Subsequently, other manifestations of the disease have been established, like skeletal, connective tissue, cardiac, and brain abnormalities[6-8].

Two forms of HIES are recognized: autosomal dominant and autosomal recessive. However, most cases of HIES are sporadic[9, 10, 16]. Diagnosis in young children can be challenging as symptoms accumulate over a period of time along with confounding clinical dilemmas.

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Case Report

A 4 month old female child with failure to thrive and global developmental delay, got admitted to the hospital with complaints of dry and scaly skin for last two months, chest wall abscess and refusal to feed for last three days. No history of fever, cough or shortness of breath. The child was hospitalised one month back for similar history of abscess over the neck and scalp, which grew staphylococcus aureus on culture and was treated with antibiotics and abscess was drained. Her birth history was uneventful. She was delivered to a 24 year old mother (P2L2) via vaginal delivery at 38 weeks with birth weight of 2.37 kg, with an uneventful neonatal period. The child was on breast feeding supplemented with formula feeds and had received only first dose of hepatitis B vaccine at birth.

On the day of admission, her vitals were stable, she was cachexic, had eczematous dermatitis, craniosynostosis, facial dysmorphism, cervical and axillary lymphadenopathy of 1 cm each and a chest wall abscess measuring 4*4 cm over left anterior chest with no signs of inflammation. Her labs on day of admission, CBC was normal with moderate eosinophilia (AEC-2600, 14%), chest wall abscess grew coagulase positive staphylococcus aureus. CSF was normal and blood culture was negative.

Her abscess was drained and treated with injectable amoxicillin clavulanic acid, according to bacterial sensitivity pattern. However, the child's condition worsened on D4, she developed respiratory distress and chest x-ray showed right upper lobe pneumonia.

Antibiotics were upgraded and in view of septicaemia, IvIg was given. After initial improvement, her respiratory distress continued to worsen on D7, when, repeat chest x ray showed features of bilateral pneumatoceles with pneumothorax. Intercostal chest tubes were put, and antifungal drugs were added as she was worsening further. Despite our best efforts, the child expired on day 10.

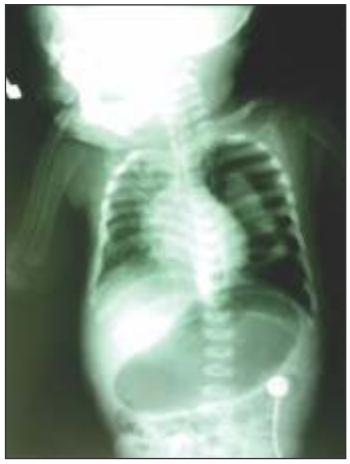

Figure 1 (left) : Chest X ray showing pneumatocoele and left pneumothorax; **Figure 2 (right) :** showing patient with facial dysmorphism, eczematous dermatitis and left chest wall abscess. Further laboratory investigations showed low CD 4, low CD3 and very low CD 8 levels, IgE levels were >2500 IU/ml. Ig A, IgG and IgM levels were within normal range.

Discussion

Clinical manifestations of HIES: Hyper IgE Syndrome usually presents very early in life. Almost all patients suffer from recurrent staphylococcal infections, beginning in infancy and predominantly involving the skin and lungs[1, 2, 11]. Newborn pustular and eczematous rashes are usually the first manifestations of the disease, typically affecting the face and scalp, with an eosinophilia and caused by *Staphylococcus aureus*. Boils are a classic finding[6].Recurrent pyogenic pneumonias are very common, starting in the childhood.

In these patients, the degree of inflammatory symptoms is variable. The "cold" abscesses, without external signs of inflammation, initially described by Davis and colleagues[4], are common. *Staphylococcus aureus* is the bacterium most frequently isolated, but *Streptococcus pneumoniae*, *Haemophilus influenzae*, enteric Gram-negative bacteria; *Candida* and *Aspergillus* are also common. Pneumonia is frequently followed by pneumatocele or bronchiectasis, which are commonly superinfected by *Aspergillus fumigatus* and *Pseudomonas aeruginosa* [12, 13]. Several cases of *pneumocystosis*, *cryptococcosis*, *histoplasmosis* and candidiasis have also been reported.

The facial appearance is very characteristic: facial asymmetry, prominent forehead, deep-set eyes, broad nasal bridge, mild prognathism, and rough appearance of the facial skin with prominent pores. Some individuals retain their primary teeth, because of the failure of those teeth to exfoliate. Other features are craniosynostosis, multiple fractures, scoliosis, Chairi I malformation, central depressions in the tongue and high arch of the palate[6, 14, 15].

Laboratory investigations: Serum IgE concentrations are extremely high in patients with HIES (> 2000 IU/ml). The molecular mechanism of hyper-IgE is unclear[3, 13]. HIES patients have normal or decreased serum IgM, IgG and IgA levels. Eosinophilia is the other consistent laboratory finding[3].Total white blood cell counts are normal but they often fail to elevate appropriately during acute infection. An impaired chemotaxis of neutrophils or monocytes has been described, a defect that explains the "cold abscesses" seen in these patients.

Therapy of hyper-IgE syndrome: There is no cure for HIES yet. The consensus favors long-term prophylactic therapy

with an anti-staphylococcal antibiotic such as trimethoprim-sulfamethoxazole[2]. The efficacy of antifungal prophylaxis remains unproven. Other options include IFN-gamma, which has inconsistent effects on IgE levels, and, Intravenous immunoglobulin, which may decrease the number of infections for some patients[17,18].

Bone marrow transplantation has been unsuccessful in this condition.

Our child had many features suggestive of Hyper IgE syndrome; eczema, recurrent staphylococcal abscess without fever and signs of inflammation, pneumonia complicated with pneumatocoele and pneumothorax, facial dysmorphism, craniosynostosis and elevated eosinophil count and IgE.

Conclusion

Patients with Hyper IgE syndrome usually die prematurely due to pulmonary infections; early diagnosis with treatment and prophylactic therapy with co-trimoxazole can be lifesaving and can lead to a significant reduction in morbidity.

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